

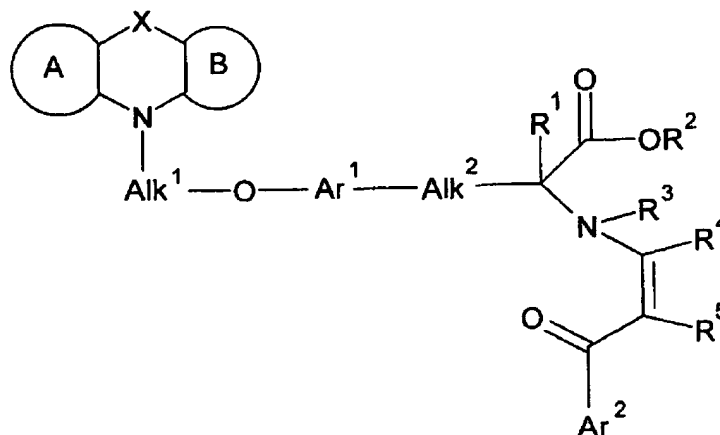
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AUG 07 2006

In the claims:

1. (Currently Amended) [[A]] An isolated compound of Formula I



wherein

ring A and ring B, fused to the ring containing X and N, independently of each other represents a 5-6 membered cyclic ring, which may optionally contain one or more heteroatoms selected from oxygen, sulfur or nitrogen atoms and may optionally substituted with one or more halogen, hydroxy, nitro, cyano, alkyl, alkenyl, [[alkenynyl,]] aralkyl, heteroarylalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, hydroxyalkyl, thioalkyl, heterocyclyl, alkoxy, aryl, aryloxy, aralkoxy, heteroaryl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, amino, alkylamino, arylamino, or aralkylamino; the ring A and ring B may be saturated or contain one or more double bonds or may be aromatic;

X is a valence bond, CH₂CH₂, CH=CH, O, S, or NR⁶ wherein R⁶ represents H, alkyl, alkenyl, [[alkenynyl,]] aralkyl, heteroarylalkyl, heterocyclyl, aryl, or heteroaryl;

R¹ is H, alkyl, alkenyl, [[alkenynyl,]] aralkyl, heteroarylalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, hydroxyalkyl, thioalkyl, heterocyclyl, OH, halogen, alkoxy, aryl, aryloxy, aralkoxy, heteroaryl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, amino, alkylamino, arylamino, or aralkylamino;

R² is H, alkyl, alkenyl, [[alkenynyl,]] aralkyl, heteroarylalkyl, heterocyclyl, aryl, or heteroaryl;

R³ is H, alkyl, alkenyl, [[alkenynyl,]] aralkyl, heteroarylalkyl, heterocyclyl, aryl, or heteroaryl;

R⁴ and R⁵ are independently H, alkyl, alkenyl, [[alkenynyl,]] aralkyl, heteroarylalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, hydroxyalkyl, thioalkyl, heterocyclyl, OH, halogen, alkoxy, aryl, aryloxy, aralkoxy, heteroaryl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, amino, alkylamino, arylamino, or aralkylamino; R⁴ and R⁵ may form a 5 or 6 membered ring optionally substituted with one or more halogen, hydroxy, nitro, cyano, alkyl, alkenyl, [[alkenynyl,]] aralkyl, heteroarylalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, hydroxyalkyl, thioalkyl, heterocyclyl, alkoxy, aryl, aryloxy, aralkoxy, heteroaryl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, amino, alkylamino, arylamino, or aralkylamino;

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Alk¹ represents C₁₋₆alkylene;

Alk² represents C₁₋₂alkylene;

Ar¹ represents arylene, hetero arylene, or a divalent heterocyclic group optionally substituted with one or more halogen, C₁₋₆alkyl, amino, hydroxy, C₁₋₆alkoxyl or aryl[[]];

Ar² represents [[an]] a substituted aryl group [[substituted]] with [[none]] one or more substituents independently selected from halogen, C₁₋₆alkyl, amino, hydroxy, C₁₋₆alkoxyl or aryl; a hetero aryl, or a heterocyclic group optionally substituted with one or more halogen, C₁₋₆alkyl, amino, hydroxy, C₁₋₆alkoxyl or aryl.

2. (Currently Amended) A compound according to claim 1, wherein

ring A is a 6 membered aromatic ring;

ring B is a 6 membered aromatic ring;

X is a valence bond, CH₂CH₂, CH=CH, O or S;

R¹ is H or alkyl;

R² is H or alkyl;

R³ is H or alkyl;

R⁴ and R⁵ are independently H or alkyl;

Alk¹ is C₂₋₃alkylene;

Alk² is C₁₋₂alkylene;

Ar¹ is an arylene group; and

Ar² is a substituted aryl group.

3. (Currently Amended) A compound according to claim 1, wherein

ring A is a 6 membered aromatic ring;

ring B is a 6 membered aromatic ring;

X is a valence bond, CH₂CH₂, CH=CH, O or S;

R¹ is H or alkyl;

R² is H or alkyl;

R³ is H or alkyl;

R⁴ and R⁵ form a 6 membered aromatic ring;

Alk¹ is C₂₋₃alkylene;

Alk² is C₁₋₂alkylene;

Ar¹ is 6 membered aromatic ring; and

Ar² is a substituted aryl group.

4. (Currently Amended) A compound according to claim 1, wherein

ring A is a benzene ring;

ring B is a benzene ring;

X is a valence bond, CH₂CH₂, CH=CH, O or S;

R¹ is H;

R² is H;

R³ is H;

R⁴ is methyl; R⁵ is H;

Alk¹ is CH₂CH₂;

Alk² is CH₂;

Ar¹ is benzene ring;

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Ar² is a substituted benzene ring [[substituted]] with [[none,]] one or more fluorine[[:]].

5. (Currently Amended) A compound according to claim 1, wherein

ring A is a benzene ring;

ring B is a benzene ring;

X is a valence bond, CH₂CH₂, CH=CH, O or S;

R¹ is H;

R² is H;

R³ is H;

R⁴ and R⁵ form a benzene ring;

Alk¹ is CH₂CH₂;

Alk² is CH₂;

Ar¹ is benzene ring;

Ar² is a substituted benzene ring [[substituted]] with [[none,]] one or more fluorine[[:]].

6. (Currently Amended) A compound according to claim 1, wherein

ring A is a benzene ring;

ring B is a benzene ring;

X is a valence bond, CH₂CH₂, CH=CH, O or S;

R¹ is H;

R² is H;

R³ is H;

R⁴ is methyl; R⁵ is H;

Alk¹ is CH₂CH₂;

Alk² is CH₂;

Ar¹ is benzene ring;

Ar² is pyridine ring substituted with none, one or more halogen.

7. (Currently Amended) A compound according to claim 1, wherein

ring A is a benzene ring;

ring B is a benzene ring;

X is a valence bond, CH₂CH₂, CH=CH, O or S;

R¹ is H;

R² is H;

R³ is H;

R⁴ and R⁵ form a benzene ring;

Alk¹ is CH₂CH₂;

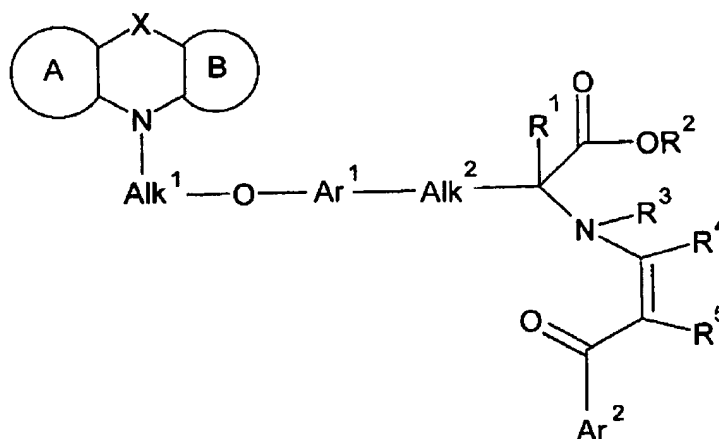
Alk² is CH₂;

Ar¹ is benzene ring;

Ar² is pyridine ring substituted with none, one or more fluorine.

8. (Currently Amended) A process for the preparation of a compound of Formula I

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(I)

wherein

ring A and ring B, fused to the ring containing X and N, independently of each other represents a 5-6 membered cyclic ring, which may optionally contain one or more heteroatoms selected from oxygen, sulfur or nitrogen atoms and may optionally substituted with one or more halogen, hydroxy, nitro, cyano, alkyl, alkenyl, [[alkenynyl,]] aralkyl, heteroarylalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, hydroxyalkyl, thioalkyl, heterocyclyl, alkoxy, aryl, aryloxy, aralkoxy, heteroaryl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, amino, alkylamino, arylamino, or aralkylamino; the ring A and ring B may be saturated or contain one or more double bonds or may be aromatic;

X is a valence bond, CH₂CH₂, CH=CH, O, S, or NR⁶ wherein R⁶ represents H, alkyl, alkenyl, [[alkenynyl,]] aralkyl, heteroarylalkyl, heterocyclyl, aryl, or heteroaryl;

R¹ is H, alkyl, alkenyl, [[alkenynyl,]] aralkyl, heteroarylalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, hydroxyalkyl, thioalkyl, heterocyclyl, OH, halogen, alkoxy, aryl, aryloxy, aralkoxy, heteroaryl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, amino, alkylamino, arylamino, or aralkylamino;

R² is H, alkyl, alkenyl, [[alkenynyl,]]

aralkyl, heteroarylalkyl, heterocyclyl, aryl, or heteroaryl;

R³ is H, alkyl, alkenyl, [[alkenynyl,]] aralkyl, heteroarylalkyl, heterocyclyl, aryl, or heteroaryl;

R⁴ and R⁵ are independently H, alkyl, alkenyl, [[alkenynyl,]] aralkyl, heteroarylalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, hydroxyalkyl, thioalkyl, heterocyclyl, OH, halogen, alkoxy, aryl, aryloxy, aralkoxy, heteroaryl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, amino, alkylamino, arylamino, or aralkylamino; R⁴ and R⁵ may form a 5 or 6 membered ring optionally substituted with one or more halogen, hydroxy, nitro, cyano, alkyl, alkenyl, [[alkenynyl,]] aralkyl, heteroarylalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, hydroxyalkyl, thioalkyl, heterocyclyl, alkoxy, aryl, aryloxy, aralkoxy, heteroaryl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, amino, alkylamino, arylamino, or aralkylamino;

Alk¹ represents C₁₋₆alkylene;

Alk² represents C₁₋₂alkylene;

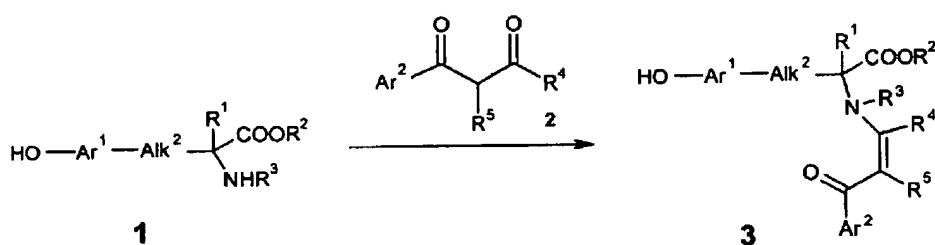
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Ar^1 represents arylene, hetero arylene, or a divalent heterocyclic group optionally substituted with one or more halogen, $[[C1-6]]$ C_{1-6} alkyl, amino, hydroxy, $[[C1-6]]$ C_{1-6} alkoxyl or aryl $[[.]]$;

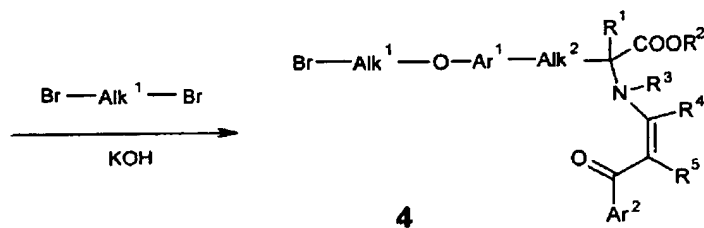
Ar^2 represents $[[an]]$ a substituted aryl group $[[substituted]]$ with $[[none,]]$ one or more substituents independently selected from halogen, $[[C1-6]]$ C_{1-6} alkyl, amino, hydroxy, $[[C1-6]]$ C_{1-6} alkoxyl or aryl; a hetero aryl, or a heterocyclic group optionally substituted with non, one or more halogen, $[[C1-6]]$ C_{1-6} alkyl, amino, hydroxy, $[[C1-6]]$ C_{1-6} alkoxyl or aryl,

a stereoisomer, enantiomer, diastereomer, hydrate or pharmaceutically acceptable salts thereof comprising the steps of:

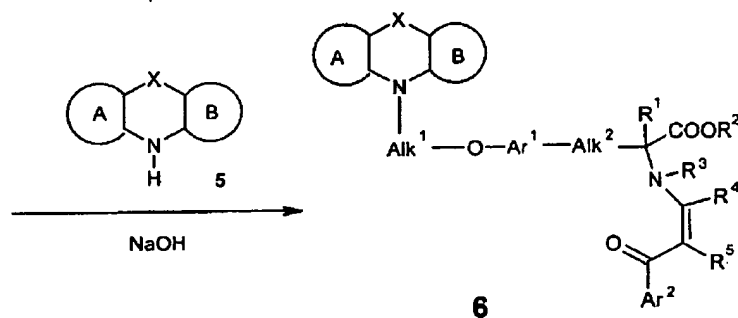
- a) initiating a condensation reaction between compound 1 and β -diketone 2 to give the vinylogous amide analogues 3;



- b) performing O-Alkylation of 3 to give compound 4;



- c) performing N-Alkylation of 4 gave the substituted arylalcanoic acid derivatives 6.



9. (Original) A process according to claim 8 wherein:

- (a) the condensation reaction is carried out in ethanol at reflux temperature;

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- (b) the O-alkylation is achieved by treatment of 3 with KOH and dibromoalkane in ethanol;
(c) the N-alkylation is achieved by treating compound 4 with NaOH and compound 5 in the presence of tetrabutyl ammonium bromide.

10-11. (Cancel)

12. (Currently Amended) A pharmaceutical composition [[for activating nuclear receptors]] comprising an effective amount of a compound according to claim 1 or its pharmaceutically acceptable salt [[with]] and at least one pharmaceutically acceptable carrier or diluent.

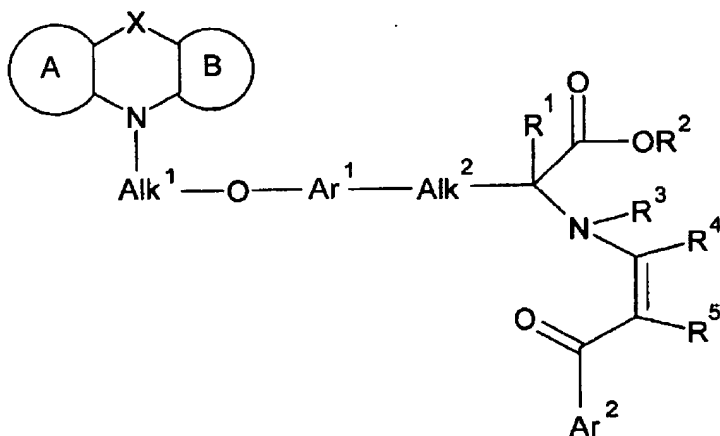
13. (Cancel)

14. (Currently Amended) The pharmaceutical composition [[of]] according to claim 12 in unit dosage form, comprising from about 0.05 to about 200 mg of the compound.

15. (Cancel)

16. (Currently Amended) The pharmaceutical composition [[of]] according to claim [[12]] 14 which is suitable for administration by an oral, nasal, transdermal, pulmonary, or parenteral route.

17. (Currently Amended) A method of treatment of [[treating or preventing]] a condition mediated by [[at least one nuclear receptor]] Peroxisome Proliferator-Activated Receptors (PPAR) comprising administering to a subject in need thereof an effective amount of a compound [[of Formula I]] according to claim 1. [[



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(I)

wherein

ring A and ring B, fused to the ring containing X and N, independently of each other represents a 5-6 membered cyclic ring, which may optionally contain one or more heteroatoms selected from oxygen, sulfur or nitrogen atoms and may optionally substituted with one or more halogen, hydroxy, nitro, cyano, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, hydroxyalkyl, thioalkyl, heterocyclyl, alkoxy, aryl, aryloxy, aralkoxy, heteroaryl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, amino, alkylamino, arylamino, or aralkylamino; the ring A and ring B may be saturated or contain one or more double bonds or may be aromatic;

X is a valence bond, CH_2CH_2 , $\text{CH}=\text{CH}$, O, S, or NR^6 wherein R^6 represents H, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, heterocyclyl, aryl, or heteroaryl;

R^1 is H, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, hydroxyalkyl, thioalkyl, heterocyclyl, OH, halogen, alkoxy, aryl, aryloxy, aralkoxy, heteroaryl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, amino, alkylamino, arylamino, or aralkylamino;

R^2 is H, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, heterocyclyl, aryl, or heteroaryl;

R^3 is H, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, heterocyclyl, aryl, or heteroaryl;

R^4 and R^5 are independently H, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, hydroxyalkyl, thioalkyl, heterocyclyl, OH, halogen, alkoxy, aryl, aryloxy, aralkoxy, heteroaryl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, amino, alkylamino, arylamino, or aralkylamino; R^4 and R^5 may form a 5 or 6 membered ring optionally substituted with one or more halogen, hydroxy, nitro, cyano, alkyl, alkenyl, alkenynyl, aralkyl, heteroarylalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, hydroxyalkyl, thioalkyl, heterocyclyl, alkoxy, aryl, aryloxy, aralkoxy, heteroaryl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, amino, alkylamino, arylamino, or aralkylamino;

Alk^1 represents C_{1-6} alkylene;

Alk^2 represents C_{1-2} alkylene;

Ar^1 represents arylene, hetero arylene, or a divalent heterocyclic group optionally substituted with one or more halogen, C_{1-6} alkyl, amino, hydroxy, C_{1-6} alkoxyl or aryl.

Ar^2 represents an aryl group substituted with none, one or more halogen, C_{1-6} alkyl, amino, hydroxy, C_{1-6} alkoxyl or aryl; a hetero aryl, or a heterocyclic group optionally substituted with one or more halogen, C_{1-6} alkyl, amino, hydroxy, C_{1-6} alkoxyl or aryl.]]

18-19. (Cancel)

20. (Currently Amended) A method of treatment of at least one [[according to claim 19 wherein said]] condition [[is]] selected from the group consisting of type 1 diabetes, type 2 diabetes, dyslipidemia, syndrome X, cardiovascular disease, atherosclerosis, hypercholesteremia, and obesity, comprising administering to a subject in need thereof an effective amount of a compound according to claim 1.

21. (Original) The method according to claim 20, wherein the effective amount of the compound is in the range of from about 0.05 to about 200 mg/kg body weight per day.

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22-28. (Cancel)

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